

**AMENDMENT TO THE CLAIMS**

Prior to continued examination, please enter the following amendments to the claims without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents as follows:

1. (Previously Presented) A centripetally-motivated microsystems platform comprising:
  - a) a rotatable platform comprising a substrate having a surface comprising a multiplicity of microfluidics structures embedded in the surface of the platform, wherein each microfluidics structure comprises
    - i) one or a plurality of aliquotted reagent reservoirs,
      - a. one or a plurality of sample reservoirs,
      - b. one or a plurality of detection reservoirs wherein each of said sample reservoir and aliquotted reagent reservoir is fluidly connected to at least one of the plurality of detection reservoirs through a microchannel, and wherein the platform further comprises
    - b) one or a plurality of bulk reagent reservoirs,
    - c) a reagent overflow reservoir and
    - d) a reagent aliquotting manifold comprising a microchannel positioned radially across the surface of the platform,

wherein the aliquotting manifold is fluidly connected to each of the plurality of aliquotted reagent reservoirs and the manifold is further fluidly connected to the overflow reservoir, and wherein fluid within the microchannels of the platform is moved through said microchannels by centripetal force arising from rotational motion of the platform for a time and a rotational velocity sufficient to move the fluid through the microchannels, the platform further comprising

e) a mixing microchannel, wherein each mixing microchannel is fluidly connected to a sample reservoir and one or a plurality of aliquotted reagent reservoirs by a microchannel, wherein the mixing microchannel defines a longitudinal path in the surface of the platform having a length sufficient to mix the sample solution and the reagent solutions to a homogenous mixture.

2. (Original) A microsystem platform of claim 1 wherein each sample reservoir further comprises a sample input port.

3. (Original) A microsystem platform of claim 1 wherein each bulk reagent reservoir further comprises a reagent input port.

4. (Original) A microsystem platform of claim 1 wherein the detection reservoirs are optically transparent.

5. (Original) A microsystem platform of claim 1 wherein each sample reservoir has a volumetric capacity of from about 1nL to about 500 $\mu$ L.

6. (Original) A microsystem platform of claim 1 wherein each reagent reservoir has a volumetric capacity of from about 1nL to about 500 $\mu$ L.

7. (Original) A microsystem platform of claim 1 wherein each detection reservoir has a volumetric capacity of from about 2nL to about 10001  $\mu$ L.

8. (Cancelled)

9. (Previously Presented) A microsystem platform of claim 1 wherein each mixing microchannel comprises a plurality of bends having angles greater than 90°.

10. (Original) A microsystem platform of claim 1 comprising from about 24 to about 10,000 microfluidics structures.

11. (Original) A microsystem platform of claim 1 wherein rotation of the platform motivates fluid through each of the microfluidics structures at a flow rate wherein the time the

fluid is in the mixing microchannel is substantially the same in each of the microfluidics structures on the platform.

12. (Original) A microsystem platform of claim 11 wherein the flow rate of fluid through each of the microfluidics structures is from about  $\ln\text{L/s}$  to about  $100\mu\text{L/s}$ .

13. (Original) A microsystem platform of claim 11 wherein the flow rate of fluid through each of the microfluidics structure is from about  $0.\ln\text{L/s}$  to about  $500\mu\text{L/s}$ .

14. (Original) A microsystem platform of claim 1 that is a circular disk.

15. (Original) The microsystem platform of Claim 1, wherein the microsystem platform is constructed of a material selected from the group consisting of an organic material, an inorganic material, a crystalline material and an amorphous material.

16. (Original) The microsystem platform of Claim 15, wherein the microsystem platform further comprises a material selected from the group consisting of silicon, silica, quartz, a ceramic, a metal or a plastic.

17. (Original) The microsystem platform of Claim 14, wherein the microsystem platform is a circular disk having a radius of about 1 to about 25cm.

18. (Original) The microsystem platform of Claim 1, wherein the microsystem platform has a thickness of about 0.1 to 100mm, and wherein the cross-sectional dimension of the microchannels embedded therein is less than 1mm and from 1 to 90 percent of said cross-sectional dimension of the platform.

19. (Original) The microsystem platform of Claim 1, wherein the microsystem platform further comprises a multiplicity of air channels, exhaust air ports and air displacement channels.

20. (Original) The microsystem platform of Claim 1, comprising a first layer and a second layer, wherein the first layer comprises sample reservoirs, bulk reagent reservoirs, aliquotted reagent reservoirs, reagent aliquotting manifold and detection reservoirs, and the second layer comprises microchannels and mixing microchannels, wherein the sample reservoirs,

bulk reagent reservoirs, aliquotted reagent reservoirs, reagent aliquotting manifold and detection reservoirs in the first layer are fluidly connected by the microchannels and mixing microchannels in the second layer when the first layer is in contact with the second layer.

21. (Original) The microsystem platform of claim 1, wherein the reagent aliquotting manifold is fluidly connected to each of the aliquotted reagent reservoirs by a microchannel having a capillary junction between the microchannel and the aliquotted reagent reservoir, and wherein the capillary junction is further connected to an air displacement channel connected to an air vent open to a surface of the platform.

22. (Original) The microsystems platform of claim 21, wherein the reagent aliquotting manifold is further fluidly connected to an overflow reservoir comprising a capillary junction, wherein rotation of the platform at a speed sufficient to overcome said capillary junction and achieve fluid flow into the overflow reservoir produces a bubble of air at the capillary junction between the microchannel connecting the reagent aliquotting manifold and the aliquotted reagent reservoir, thereby preventing fluid flow into said aliquotted reagent reservoir.

23. (Original) The microsystem platform of claim 2 comprising a plurality of sample reservoirs each having a sample input port, wherein the plurality of sample input ports are arranged on the surface of the platform to be adapted to the conformation of a robotic or automated pipettor.

24. (Original) A centripetally-motivated fluid micromanipulation apparatus that is a combination of

a microsystem platform according to claim 1, and

a micromanipulation device, comprising a base, a rotating means, a power supply and user interface and operations controlling means, wherein the rotating means is operatively linked to the microsystem platform and in rotational contact therewith

wherein a volume of a fluid within the microchannels of the platform is moved through said microchannels by centripetal force arising from rotational motion of the platform for a time and a rotational velocity sufficient to move the fluid through the microchannels.

25-31. (Canceled)

32. (Original) A method for homogenously mixing a sample and one or a plurality of reagents, comprising the steps of:

- a) applying a volume of a fluid comprising a biological sample to one or a plurality of sample reservoirs of a microsystem platform of claim 1 when the platform is stationary, wherein the biological sample applied to each sample reservoir is the same or different;
- b) applying a volume of a solution comprising a reagent to a bulk reagent reservoir of a microsystem platform of claim 1 when the platform is stationary;
- c) rotating the platform at a first rotational speed sufficient to motivate fluid flow from the bulk reagent reservoir into the reagent aliquotting manifold of a microsystem platform of claim 1 and delivering an amount of reagent into each of a plurality of aliquotted reagent reservoirs
- d) rotating the platform at a second rotational speed sufficient to motivate fluid flow from each sample reservoir and one or a plurality of reagent reservoirs into a mixing microchannel, wherein the platform is rotated for a time sufficient for the sample volume and reagent volume to traverse the mixing microchannel and be homogeneously mixed;
- e) delivering the mixture of the homogeneous mixture of the sample volume and reagent volume to a detection reservoir; and
- f) detecting the homogenous mixture or reaction product produced therein.

33. (Original) A method according to claim 32, wherein a component of the biological sample reacts with one or a plurality of reagents in the homogeneous mixture.

34. (Original) A method according to claim 33, wherein a component of the biological sample reacts with one or a plurality of reagents in the homogeneous mixture to form a reaction product, and the reaction product is detected.

35. (Original) A method according to claim 32, wherein the biological sample comprises an enzymatic species.

36. (Original) A method for performing a biological or biochemical reaction, comprising the steps of:

- a) applying a volume of a fluid comprising a biological sample to one or a plurality of sample reservoirs of a microsystem platform of claim 1 when the platform is stationary, wherein the biological sample applied to each sample reservoir is the same or different and wherein the biological sample comprises one component of the biological or biochemical reaction;
- b) applying a volume of a solution comprising a reagent to a bulk reagent reservoir of a microsystem platform of claim 1 when the platform is stationary, wherein one or a plurality of reagents comprises another component of the biological or biochemical reaction;
- c) rotating the platform at a first rotational speed sufficient to motivate fluid flow from the bulk reagent reservoir into the reagent aliquotting manifold of a microsystem platform of claim 1 and delivering an amount of reagent into each of a plurality of aliquotted reagent reservoirs
- d) rotating the platform at a second rotational speed sufficient to motivate fluid flow from each sample reservoir and one or a plurality of reagent reservoirs into a mixing microchannel, wherein the platform is rotated for a time sufficient for the sample volume and reagent volume to traverse the mixing microchannel and be homogeneously mixed;

- e) delivering the mixture of the homogeneous mixture of the sample volume and reagent volume to a detection reservoir, and
- f) detecting a product of the biological or biochemical reaction.

37. (Original) A method according to claim 36, wherein the biological sample comprises an enzymatic species.

38. (Original) A microsystem platform of claim 23, wherein the sample input ports are arranged in the surface of the platform in a rectangular pattern having a spacing that is adapted for an 8-tip linear or 96-tip rectangular pipetting device.

39. (Original) A microsystem platform of claim 38, wherein the sample input ports are arranged in the surface of the platform having a space of 9mm, 4.5mm or 2.25mm between individual entry ports.

40. (Original) A microsystem platform of claim 23, wherein the sample input ports are arranged in the surface of the platform in a rectangular pattern of 8 x 12, 16 x 24 or 32 x 48 elements.

41. (Original) A centripetally-motivated microsystems platform comprising:

a rotatable platform comprising a substrate having a surface comprising a one or a multiplicity of microfluidics structures embedded in the surface of the platform, wherein each microfluidics structure comprises

a plurality of cell culture chambers, and one or a plurality of overflow reservoirs at least two reagent reservoirs and a branching dilution microchannel comprising a multiplicity of branches fluidly connected to capillary junctions

wherein each of said cell culture chambers is fluidly connected to at least one of the reagent reservoirs through the branching dilution microchannel and wherein the branching dilution microchannel is fluidly connected to each of the reagent reservoirs,

wherein fluid within the branching dilution microchannel is moved through said microchannel by centripetal force arising from rotational motion of the platform for a time and a rotational velocity sufficient to move the fluid through the microchannel and wherein a portion of the fluid flow from each of the reagent reservoirs flow directly through the branched dilution microchannel into each of the cell culture chambers, and wherein a portion of the fluid flow through the branching dilution microchannel flows through each of the capillary junctions into a separate branch of the branching dilution microchannel, wherein each branch of the branching dilution microchannel is fluidly connected to one cell culture chamber and each branch contains a mixture of fluid from each of the reagent reservoirs in different proportions of the fluids.

Please add the following new claims:

42. (New) A centripetally-motivated microsystems platform comprising:

- a) a rotatable platform comprising a substrate having a surface comprising a multiplicity of microfluidics structures embedded in the surface of the platform, wherein each microfluidics structure comprises
  - i) one or a plurality of aliquotted reagent reservoirs,
  - ii) one or a plurality of sample reservoirs, each sample reservoir comprising a sample input port,
  - iii) one or a plurality of detection reservoirs, wherein each of said sample reservoir and aliquotted reagent reservoir is fluidly connected to at least one of the plurality of detection reservoirs through a microchannel; andwherein the platform further comprises
- b) one or a plurality of bulk reagent reservoirs,
- c) a reagent overflow reservoir, and
- d) a reagent aliquotting manifold comprising a microchannel positioned radially across the surface of the platform,

wherein the aliquotting manifold is fluidly connected to each of the plurality of aliquotted reagent reservoirs and the manifold is further fluidly connected to the overflow reservoir, wherein the sample input ports are arranged on the surface of the platform in a pattern of



24 or 96, or 384, or 1536 elements to be adapted to the conformation of the pipette tips of a robotic or automated pipetter, and wherein fluid within the microchannels of the platform is moved through said microchannels by centripetal force arising from rotational motion of the platform for a time and a rotational velocity sufficient to move the fluid through the microchannels.

43. (New) The microsystems platform of claim 42, wherein each bulk reagent reservoir further comprises a reagent input port.

44. (New) The microsystems platform of claim 42, wherein the detection reservoirs are optically transparent.

45. (New) The microsystems platform of claim 42, wherein each sample reservoir and each reagent reservoir has a volumetric capacity of from 1 nl to 500  $\mu$ l and each detection reservoir has a volumetric capacity of from 2 nl to 1000  $\mu$ l.

46. (New) The microsystems platform of claim 42, wherein the microsystems platform further comprises mixing microchannels, wherein each mixing microchannel is fluidly connected to a sample reservoir and one or a plurality of aliquotted reagent reservoirs by a microchannel, wherein the mixing microchannel defines a longitudinal path in the surface of the platform having a length sufficient to mix the sample solution and the reagent solutions to a homogenous mixture.

47. (New) The microsystems platform of claim 46, wherein each mixing microchannel comprises a plurality of bends having angles greater than 90°.

48. (New) The microsystems platform of claim 42, wherein the microsystems platform is a circular disk having a radius of 1 to 25 cm rotation of which motivates fluid through each of the microfluidics structures at a flow rate, wherein the time the fluid is in the mixing microchannel is substantially the same in each of the microfluidics structures on the platform.

49. (New) The microsystems platform of claim 48, wherein the flow rate of fluid through each of the microfluidics structures is from 0.1 nl/s to 500  $\mu$ l/s.

50. (New) The microsystems platform of claim 42, wherein the microsystems platform has a thickness of 0.1 mm to 100 mm, and wherein the crosssectional dimension of the microchannels embedded therein is less than 1 mm and from 1 to 90 % of said crosssectional dimension of the platform.

51. (New) The microsystems platform of claim 42, comprising a first layer and a second layer, wherein the first layer comprises sample reservoirs, bulk reagent reservoirs, aliquotted reagent reservoirs, reagent aliquotting manifold and detection reservoirs, and the second layer comprises microchannels and mixing microchannels, wherein the sample reservoirs, bulk reagent reservoirs, aliquotted reagent reservoirs, reagent aliquotting manifold and detection reservoirs in the first layer are fluidly connected by the microchannels and mixing microchannels in the second layer when the first layer is in contact with the second layer.

52. (New) The microsystems platform of claim 42, wherein the reagent aliquotting manifold is fluidly connected to each of the aliquotted reagent reservoirs by a microchannel having a capillary junction between the microchannel and the aliquotted reagent reservoir, and wherein the capillary junction is further connected to an air displacement channel connected to an air vent open to a surface of the platform.

53. (New) The microsystems platform of claim 52, wherein the reagent aliquotting manifold is further fluidly connected to an overflow reservoir comprising a capillary junction, wherein rotation of the platform at a speed sufficient to overcome said capillary junction and achieve fluid flow into the overflow reservoir produces a bubble of air at the capillary junction between the microchannel connecting the reagent aliquotting manifold and the aliquotted reagent reservoir, thereby preventing fluid flow into said aliquotted reagent reservoir.

54. (New) The microsystems platform of claim 42, comprising a plurality of sample reservoirs each having a sample input port wherein the sample input ports are arranged on the surface of the platform in a rectangular pattern having a spacing that is adapted for an 8-tip linear or 96-tip rectangular pipetting device.

55. (New) The microsystems platform of claim 54, wherein the sample input ports are arranged in the surface of the platform having a space of 9 mm, or 4.5 mm, or 2.25 mm between individual entry ports.

56. (new) The microsystems platform of claim 54, wherein the sample input ports are arranged in the surface of the platform in a rectangular pattern of 8x12, 16x24 or 32x48 elements.